UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,458	09/10/2003	Gary W. Pace	8703-510	7151

61834 7590 04/15/2009

Ostrow Kaufman & Frankl LLP
Susan Formicola
The Chrysler Building
405 Lexington Avenue, 62nd Floor
NEW YORK, NY 10174

EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
04/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,458	PACE ET AL.	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-37 have been cancelled. Claims 38-45 are new. Applicant's amendments have necessitated a new ground of rejection. Accordingly, this Action is FINAL.

Withdrawn rejections:

Applicant's amendments and arguments filed 9/29/08 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn. Claims 1-3, 7, 17-19, 24-26, 29-33, 36 and 37 were rejected under 35 U.S.C. 102(b) as being anticipated by Ross et al. (Pain 2000, 84, 421-428). It is unknown if the rats of Ross had a respiratory illness. Therefore, the Examiner withdraws the rejection. Claims 1-3, 5, 7, 10, 11, 17-19 and 24-37 were rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al. (WO 97/14438). The patients of Smith et al. did not have a respiratory illness. The rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 39 introduces new matter as the claims recites the limitation "a ratio of morphine to oxycodone of 1:0.66 to 1:2.0 by weight" There is no support in the specification for this limitation. The limitation of "a ratio of morphine to oxycodone of 1:0.66 to 1:2.0 by weight" was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. The specification teachs "ratios of about 1 to 0.66 by weight of about 1 to 2.0 by weight" in [0075] but does not describe the instantly claimed limitation. The ratio of 1.0:0.66 and 1:2.0 are individually taught in [0066, 0067 and 0074] but the range is not taught and represents a new concept. There is no guidance in the specification to select a ratio of morphine to oxycodone of 1:0.66 to 1:2.0 by weight. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 38-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mercer, M. Anaesthesia for the Patient with Respiratory Disease (Practical Procedures 2000, 12, 15 pages) in view of Smith et al. (US 6,310,072).

Applicant claims a method for treating a human with a respiratory illness for the alleviation or prevention of pain, said method comprising administering to the human with the respiratory illness a sub-analgesic dose of morphine or a pharmaceutically acceptable salt thereof, and a sub- analgesic dose of oxycodone or a pharmaceutically acceptable salt thereof, whereby said treatment produces an analgesic effect in the human and the human experiences a reduced level of respiratory depression than

associated with a dosage of morphine or oxycodone required to achieve the same analgesic effect.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Mercer teaches methods of treating a patient with underlying respiratory disease is at increased risk of postoperative pulmonary complications with opioid analgesics and that pain relief, effective analgesia, reduces the incidence of postoperative respiratory complications, but that respiratory depression is observed for and prevented (pages 1, 2, 10, and 11 of 15). Low doses of opioids in an epidural infusion results in the best analgesia for the fewest side effects (page 11 of 15). Tuberculosis, bronchiectasis pneumonia, emphysema, COPD, infection and asthma are mentioned as restrictive pulmonary diseases and postoperative respiratory problems (pages 4, 6, 7, 8, 11, and 12-14 of 15). Mercer teaches that sleep apnea, a sleep disorder, may lead to post operative airway compromise (page 2 of 15).

Smith et al. teach

72. A method for producing analgesia in humans and lower animals which comprises administering concurrently to a human or lower animal in need of such treatment a composition comprising a sub-analgesic dosage of a μ-opioid agonist selected from the group consisting of morphine, fentanyl, sufentanil, alfentanil and hydromorphone, or a pharmaceutically acceptable salt thereof, and a sub-analgesic dosage of oxycodone which is a κ_2-opioid agonist or a pharmaceutically acceptable salt thereof.

73. A method as claimed in claim **72** wherein the μ-opioid agonist is in the form of a pharmaceutically acceptable salt.

74. A method as claimed in claim **72** wherein the μ-opioid agonist is morphine.

Smith et al. teach

mg/kg and about 5 mg/kg every three to six hours.

143. A method as claimed in claim **72** wherein the mode of administering the composition is selected from the group consisting of oral, rectal, parenteral, sublingual, buccal, intrathecal, epidural, intravenous, intra-articular, intramuscular, intradermal, subcutaneous, inhalational, intraocular, intraperitoneal, intracerebroventricular and transdermal.

Since Smith et al. use the same sub-analgesic amounts as claimed, then the method of Smith et al. intrinsically produces a reduced level of respiratory depression. Smith et al. teach various administration routes, including oral, parenteral, subcutaneous and intravenous, and controlled-release dosage forms reading on instant claim 43 (see claims 143 and 155). It is the Examiner's position, in the absence of evidence to the contrary, that Smith et al. make the distinction between immediate

release oral dosing and sustained release oral dosing and thus reads on instant claim 10 and 26-28. Smith et al. teach dosages between about 0.5 and about 3.5 mg morphine and between about 1.0 and about 8.0 mg oxycodone (column lines and column 7, lines 25-30).

Smith et al. teach a wide range of dosages in claims 72-145 reading on instant claims 39-41.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. The difference between the instant application and Mercer is that Mercer do not expressly teach sub-analgesic amounts of morphine and oxycodone in the method of treating a human with a respiratory illness. This deficiency in Mercer is cured by the teachings of Smith et al.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of producing analgesia as taught by Smith et al. in the method of Mercer et al and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Mercer instructs the use of low doses of the opioids in order to avoid adverse side

effects such as respiratory depression and Smith et al. provide an analgesic method using sub-analgesic amounts of the compounds which would avoid the respiratory depression taught by Mercer. Regarding the limitations of instant claims 40 and 41, the U.S. Patent Office is not equipped with analytical instruments to test prior art compositions for the infinite number of ways that a subsequent applicant may present previously unmeasured characteristics. When as here, the prior art appears to contain the exact same sub-analgesic amounts of ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is properly shifted to applicant to show otherwise. With regard to the other respiratory illnesses in claim 44, such illnesses are obvious to one of ordinary skill in the art of respiratory illnesses, in the absence of evidence to the contrary.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ernst V Arnold/
Examiner, Art Unit 1616